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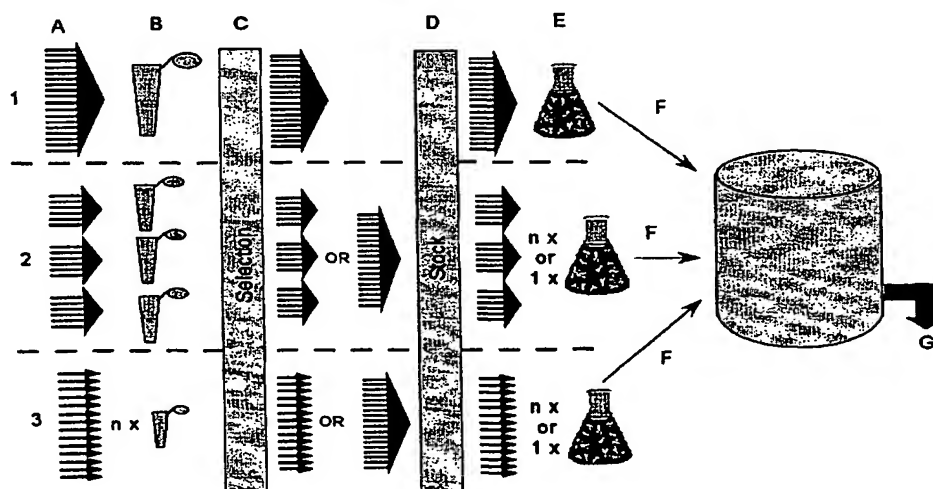
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[Continued on next page]

(54) Title: METHOD FOR MANUFACTURING RECOMBINANT POLYCLONAL PROTEINS



(57) Abstract: The invention relates to a method for manufacturing a recombinant polyclonal protein composition, in particular a recombinant polyclonal antibody composition. The method comprises obtaining a collection of cells transfected with a library of variant nucleic acid sequences, wherein each cell in the collection is transfected with and capable of expressing one member of the library, which encodes a distinct member of a polyclonal protein that binds a particular antigen and which is located at the same single site in the genome of individual cells in said collection, wherein said nucleic acid sequence is not naturally associated with said cell in the collection. The cells are cultured under suitable conditions for expression of the polyclonal protein, which is obtained from the cells or culture supernatant. The nucleic acid sequence is introduced into the cells by transfection with a library of vectors for site-specific integration. The present method is suitable for manufacturing recombinant polyclonal antibodies, thereby making available a superior replacement of plasma-derived therapeutic immunoglobulin products.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS, CHEM ABS Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/055718 A (HUA SHAOBING BENJAMIN ; LIN YU-HUEI (US); GENETASTIX CORP (US); SHERID) 18 July 2002 (2002-07-18)	41, 42
Y	page 7, line 19 - line 24 page 17, line 28 - page 18, line 22 page 21, line 8 - line 25 page 64, line 23 - page 66, line 13	1-40
Y	WO 02/44361 A (HUSE WILLIAM D ; APPLIED MOLECULAR EVOLUTION IN (US)) 6 June 2002 (2002-06-06) page 10, line 15 - line 32 page 16, line 4 - page 18, line 15 page 32, line 16 - page 33, line 24 page 42, line 25 - line 30 claims 1-40	1-40
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *&* document member of the same patent family

Date of the actual completion of the international search

14 September 2004

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Mandl, B

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International Application No.

DK2004/000001

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 789 208 A (SHARON JACQUELINE) 4 August 1998 (1998-08-04) abstract column 17, line 21 - line 64 column 18, line 29 - line 34 -----	41-47
X	WO 01/89563 A (SYMPHOGEN AS) 29 November 2001 (2001-11-29) abstract; claims 1-24 -----	41, 43, 45, 46
A	US 5 677 177 A (WAHL GEOFFREY M ET AL) 14 October 1997 (1997-10-14) cited in the application abstract claims 1-24 -----	1-40
A	WO 00/11155 A (UNIV LELAND STANFORD JUNIOR) 2 March 2000 (2000-03-02) abstract; claims 1-71 -----	1-47
A	SODERLIND E ET AL: "Recombining germline-derived CDR sequences for creating diverse single-framework antibody libraries" NATURE BIOTECHNOLOGY, vol. 18, no. 8, August 2000 (2000-08), pages 852-856, XP002242392 ISSN: 1087-0156 cited in the application the whole document -----	1-47
A	WO 98/41645 A (IDEC PHARMA CORP) 24 September 1998 (1998-09-24) cited in the application the whole document -----	1-47

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International application No.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 43 and 44 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

DK2004/000001

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